

WEST Search History

DATE: Thursday, February 20, 2003

<u>Set Name</u> side by side	<u>Query</u>	<u>Hit Count</u>	<u>Set Name</u> result set
<i>DB=USPT,PGPB,JPAB,EPAB,DWPI; PLUR=YES; OP=ADJ</i>			
L10	5597719.pn.	2	L10
L9	5869308.pn.	2	L9
L8	5656612.pn.	2	L8
L7	L6 and angiogene\$	0	L7
L6	raf-caax	4	L6
L5	5952229.pn.	2	L5
L4	5952229	11	L4
L3	L1 with angiogene\$	23	L3
L2	L1 near10 angiogene\$	8	L2
L1	raf	2315	L1

END OF SEARCH HISTORY

WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 1 through 10 of 23 returned.**☐ 1. Document ID: US 20030017573 A1

L3: Entry 1 of 23

File: PGPB

Jan 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030017573

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030017573 A1

TITLE: Polymerase kappa compositions and methods thereof

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Friedberg, Errol C.	Dallas	TX	US	
Gerlach, Valerie	Branford	CT	US	
Feaver, William J.	Branford	CT	US	

US-CL-CURRENT: 435/226; 435/320.1, 435/325, 435/69.1, 536/23.2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw Desc	Image
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☐ 2. Document ID: US 20030013674 A1

L3: Entry 2 of 23

File: PGPB

Jan 16, 2003

PGPUB-DOCUMENT-NUMBER: 20030013674

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030013674 A1

TITLE: Use of targeted cross-linked nanoparticles for in vivo gene delivery

PUBLICATION-DATE: January 16, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Bednarski, Mark D.	Los Altos	CA	US	
Guccione, Samira	Hillsborough	CA	US	
Li, King Chuen	Bethesda	MD	US	

US-CL-CURRENT: 514/44; 424/499

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments	Claims	KMC	Draw Desc	Image
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☐ 3. Document ID: US 20030004351 A1

L3: Entry 3 of 23

File: PGPB

Jan 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030004351
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030004351 A1

TITLE: Substituted oxindole derivatives as protein tyrosine kinase and as protein serine/threonine kinase inhibitors

PUBLICATION-DATE: January 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Davis, Stephen Thomas	Durham	NC	US	
Dickerson, Scott Howard	Chapel Hill	NC	US	
Frye, Stephen Vernon	Durham	NC	US	
Harris, Philip Anthony	Raleigh	NC	US	
Hunter, Robert Neil III	Raleigh	NC	US	
Kuyper, Lee Frederick	Durham	NC	US	
Lackey, Karen Elizabeth	Hillsborough	NC	US	
Luzzio, Michael Joseph	Groton	CT	US	
Veal, James Marvin	Apex	NC	US	
Walker, Duncan Herrick	Summit	NJ	US	

US-CL-CURRENT: 546/200; 548/361.1, 548/432, 548/486

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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4. Document ID: US 20030004350 A1

L3: Entry 4 of 23

File: PGPB

Jan 2, 2003

PGPUB-DOCUMENT-NUMBER: 20030004350
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030004350 A1

TITLE: AZAINDOLE DERIVATIVES, PROCESS FOR THEIR PREPARATION, AND THEIR USE AS ANTITUMOR AGENTS

PUBLICATION-DATE: January 2, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Longo, Antonio	Milan		IT	
Brasca, Maria Gabriella	Cusago		IT	
Orsini, Paolo	Gallarate		IT	
Traquandi, Gabriella	Milan		IT	
Pittala, Valeria	Catania		IT	
Vulpetti, Anna	Brugherio		IT	
Varasi, Mario	Milan		IT	
Pevarello, Paolo	Pavia		IT	

US-CL-CURRENT: 546/113

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 5. Document ID: US 20020192665 A1

L3: Entry 5 of 23

File: PGPB

Dec 19, 2002

PGPUB-DOCUMENT-NUMBER: 20020192665
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020192665 A1

TITLE: Compositions and methods for the therapeutic use of an atonal-associated sequence for a gastrointestinal condition

PUBLICATION-DATE: December 19, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Zoghbi, Huda Y.	Houston	TX	US	
Yang, Qi	The Woodlands	TX	US	

US-CL-CURRENT: 435/6; 435/366, 435/7.21

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 6. Document ID: US 20020187105 A1

L3: Entry 6 of 23

File: PGPB

Dec 12, 2002

PGPUB-DOCUMENT-NUMBER: 20020187105
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020187105 A1

TITLE: Polymer combinations that result in stabilized aerosols for gene delivery to the lungs

PUBLICATION-DATE: December 12, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Zou, Yiyu	Bronx	NY	US	
Perez-Soler, Roman	New York	NY	US	

US-CL-CURRENT: 424/45; 424/78.38, 514/2

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 7. Document ID: US 20020156081 A1

L3: Entry 7 of 23

File: PGPB

Oct 24, 2002

PGPUB-DOCUMENT-NUMBER: 20020156081
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020156081 A1

TITLE: Pyrazolopyrimidines as therapeutic agents

PUBLICATION-DATE: October 24, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Hirst, Gavin C.	Marlborough	MA	US	
Rafferty, Paul	Westborough	MA	US	
Ritter, Kurt	Newton	MA	DE	
Calderwood, David	Framingham	MA	GB	
Wishart, Neil	Jefferson		US	
Arnold, Lee D.	Westborough		CA	
Friedman, Michael M.	Newton		US	

US-CL-CURRENT: 514/247; 514/249, 544/237, 544/262

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KIMC	Draw Desc	Image
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8. Document ID: US 20020151060 A1

L3: Entry 8 of 23

File: PGPB

Oct 17, 2002

PGPUB-DOCUMENT-NUMBER: 20020151060
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020151060 A1

TITLE: PEI: DNA vector formulations for in vitro and in vivo gene delivery

PUBLICATION-DATE: October 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Cristiano, Richard J.	Pearland	TX	US	
Yamashita, Motoyuki	Kochi City		JP	

US-CL-CURRENT: 435/455; 424/486, 514/44

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KIMC	Draw Desc	Image
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9. Document ID: US 20020143062 A1

L3: Entry 9 of 23

File: PGPB

Oct 3, 2002

PGPUB-DOCUMENT-NUMBER: 20020143062
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020143062 A1

TITLE: Method to incorporate N-(4-hydroxyphenyl) retinamide in liposomes

PUBLICATION-DATE: October 3, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Lopez-Berestein, Gabriel	Bellaire	TX	US	
Tari, Ana M.	Houston	TX	US	
Lim, Soo-Jeong	Seoul		KR	

US-CL-CURRENT: 514/613; 424/155.1, 424/450

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KIMC	Draw Desc	Image
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10. Document ID: US 20020137731 A1

L3: Entry 10 of 23

File: PGPB

Sep 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020137731

PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20020137731 A1

TITLE: Combination of radiation and vitamin D3 analogs for the treatment of cancer

PUBLICATION-DATE: September 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Gewirtz, David A.	Richmond	VA	US	

US-CL-CURRENT: 514/167; 600/1

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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RAMC	Draw Desc	Image
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L3: Entry 11 of 23

File: PGPB

Aug 8, 2002

PGPUB-DOCUMENT-NUMBER: 20020106348
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020106348 A1

TITLE: Cancer therapeutics involving the administration of 2-methoxyestradiol and an agent that increases intracellular superoxide anion

PUBLICATION-DATE: August 8, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Huang, Peng	Houston	TX	US	
Plunkett, William K.	Houston	TX	US	
Feng, Li	Sugar Land	TX	US	

US-CL-CURRENT: [424/85.1](#); [514/182](#), [514/34](#), [514/72](#), [514/8](#)

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#)[KMC](#) | [Draw Desc](#) | [Image](#)**12. Document ID: US 20020028815 A1**

L3: Entry 12 of 23

File: PGPB

Mar 7, 2002

PGPUB-DOCUMENT-NUMBER: 20020028815
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020028815 A1

TITLE: Novel multicyclic compounds and the use thereof

PUBLICATION-DATE: March 7, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY	RULE-47
Ator, Mark A.	Paoli	PA	US	
Bihovsky, Ron	Wynnewood	PA	US	
Chatterjee, Sankar	Wynnewood	PA	US	
Dunn, Derek	Thorndale	PA	US	
Hudkins, Robert L.	Chester Springs	PA	US	

US-CL-CURRENT: [514/249](#); [514/290](#), [514/373](#), [514/411](#), [544/234](#), [546/79](#), [548/207](#), [548/427](#)

[Full](#) | [Title](#) | [Citation](#) | [Front](#) | [Review](#) | [Classification](#) | [Date](#) | [Reference](#) | [Sequences](#) | [Attachments](#)[KMC](#) | [Draw Desc](#) | [Image](#)

☐ 13. Document ID: US 6503914 B1

L3: Entry 13 of 23

File: USPT

Jan 7, 2003

US-PAT-NO: 6503914

DOCUMENT-IDENTIFIER: US 6503914 B1

TITLE: Thienopyrimidine-based inhibitors of the Src family

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KM/C	Draw Desc	Image
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☐ 14. Document ID: US 6486322 B1

L3: Entry 14 of 23

File: USPT

Nov 26, 2002

US-PAT-NO: 6486322

DOCUMENT-IDENTIFIER: US 6486322 B1

TITLE: Azaindole derivatives, process for their preparation, and their use as antitumor agents

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KM/C	Draw Desc	Image
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☐ 15. Document ID: US 6455559 B1

L3: Entry 15 of 23

File: USPT

Sep 24, 2002

US-PAT-NO: 6455559

DOCUMENT-IDENTIFIER: US 6455559 B1

TITLE: Phenylacetamido-pyrazole derivatives, process for their preparation and their use as antitumor agents

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KM/C	Draw Desc	Image
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☐ 16. Document ID: US 6455525 B1

L3: Entry 16 of 23

File: USPT

Sep 24, 2002

US-PAT-NO: 6455525

DOCUMENT-IDENTIFIER: US 6455525 B1

TITLE: Heterocyclic substituted pyrazolones

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KM/C	Draw Desc	Image
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☐ 17. Document ID: US 6414013 B1

L3: Entry 17 of 23

File: USPT

Jul 2, 2002

US-PAT-NO: 6414013

DOCUMENT-IDENTIFIER: US 6414013 B1

TITLE: Thiophene compounds, process for preparing the same, and pharmaceutical

compositions containing the same background of the invention

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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☐ 18. Document ID: US 6387919 B1

L3: Entry 18 of 23

File: USPT

May 14, 2002

US-PAT-NO: 6387919

DOCUMENT-IDENTIFIER: US 6387919 B1

TITLE: Substituted oxindole derivatives as protein tyrosine kinase and as protein serine/threonine kinase inhibitors

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 19. Document ID: US 6369086 B1

L3: Entry 19 of 23

File: USPT

Apr 9, 2002

US-PAT-NO: 6369086

DOCUMENT-IDENTIFIER: US 6369086 B1

TITLE: Substituted oxindole derivatives as protein tyrosine and as protein serine/threonine kinase inhibitors

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 20. Document ID: US 6335342 B1

L3: Entry 20 of 23

File: USPT

Jan 1, 2002

US-PAT-NO: 6335342

DOCUMENT-IDENTIFIER: US 6335342 B1

TITLE: Azaindole derivatives, process for their preparation, and their use as antitumor agents

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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WEST[Generate Collection](#)[Print](#)**Search Results - Record(s) 21 through 23 of 23 returned.**☐ 21. Document ID: US 6268391 B1

L3: Entry 21 of 23

File: USPT

Jul 31, 2001

US-PAT-NO: 6268391

DOCUMENT-IDENTIFIER: US 6268391 B1

TITLE: Benzylidene-1,3-dihydro-indol-2-one derivatives a receptor tyrosine kinase inhibitors, particularly of Raf kinases

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 22. Document ID: US 6410518 B1

L3: Entry 22 of 23

File: DWPI

Jun 25, 2002

DERWENT-ACC-NO: 2002-597918

DERWENT-WEEK: 200264

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TITLE: Treating cancer, angiogenesis or neovascularization by administering antisense oligonucleotides targeted to human raf sequences

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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KWIC	Draw Desc	Image
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☐ 23. Document ID: KR 2002032553 A WO 200112210 A1 AU 200067633 A EP 1210099 A1 NO 200200718 A SK 200200214 A3 CZ 200200449 A3

L3: Entry 23 of 23

File: DWPI

May 3, 2002

DERWENT-ACC-NO: 2001-202826

DERWENT-WEEK: 200270

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TITLE: Composition for modulating angiogenesis and treating rheumatoid arthritis and restenosis comprises Raf protein or viral or non-viral gene transfer vector containing nucleic acid encoding for Raf or Ras protein

Full	Title	Citation	Front	Review	Classification	Date	Reference	Sequences	Attachments
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**BENZYLIDENE-1,3-DIHYDRO-INDOL-2-ONE
DERIVATIVES A RECEPTOR TYROSINE
KINASE INHIBITORS, PARTICULARLY OF
RAF KINASES**

FIELD OF THE INVENTION

The present invention provides novel compounds, novel compositions, methods of their use and methods of their manufacture, such compounds generally pharmacologically useful as agents in those disease states alleviated by the alteration of mitogen activated signalling pathways in general, and in particular the inhibition or antagonism of protein kinases, which pathologically involve aberrant cellular proliferation, such disease states including tumor growth. The aforementioned pharmacologic activities are useful in the treatment of mammals. In particular, the invention relates to benzylidene oxindole derivatives which exhibit cRaf-1 kinase inhibition for the treatment of disorders related to cell proliferation.

More specifically, the compounds of the present invention can be used in the treatment of certain forms of cancer, can be used to provide additive or synergistic effects with certain existing cancer chemotherapies, and/or used to restore effectiveness of certain existing cancer chemotherapies and radiation. At the present time, there is a need in the areas of diseases characterized by cell proliferation for such therapeutic agents.

BACKGROUND OF THE INVENTION

Cancer results from the deregulation of the normal processes that control cell division, differentiation and apoptotic cell death. Protein kinases play a critical role in this regulatory process. A partial non-limiting list of such kinases includes ab1, ATK, bcr-ab1, Blk, Brk, Btk, c-kit, c-met, c-src, CDK1, CDK2, CDK4, CDK6, cRaf1, CSF1R, CSK, EGFR, ErbB2, ErbB3, ErbB4, ERK, Fak, fes, FGFR1, FGFR2, FGFR3, FGFR4, FGFR5, Fgr, FLK4, flt-1, Fps, Frk, Fyn, Hck, IGF-1R, INS-R, Jak, KDR, Lck, Lyn, MEK, p38, PDGFR, PIK, PKC, PYK2, ros, tie₁, tie₂, TRK, Yes and Zap70. In mammalian biology, such protein kinases comprise mitogen activated protein kinase (MAPK) signalling pathways. MAPK signalling pathways are inappropriately activated by a variety of common disease-associated mechanisms such as mutation of ras genes and deregulation of growth factor receptors (Magnuson et al, *Seminars in Cancer Biology*; 1994 (5), 247-252). Therefore the inhibition of protein kinases is an object of the present invention.

Additionally, protein kinases have been implicated as targets in central nervous system disorders (such as Alzheimer's), inflammatory disorders (such as psoriasis), bone diseases (such as osteoporosis), atheroscleroses, restenosis, thrombosis, metabolic disorders (such as diabetes) and infectious diseases (such as viral and fungal infections).

One of the most commonly studied pathways involving kinase regulation is cellular signalling from receptors at the cell surface to the nucleus (Crews and Erikson, 1993). One example of this pathway includes a cascade of kinases in which members of the Growth Factor receptor Tyrosine Kinases (such as EGF-R, PDGF-R, VEGF-R, IGF1-R, the Insulin receptor), deliver signals through phosphorylation to other kinases such as Src Tyrosine kinase, and the Raf, Mek and Erk serine/threonine kinase families (Crews and Erikson, 1993; Ihle et al., 1994). Each of these kinases is represented by several family members (Pelech and Sanghera, 1992) which play related, but functionally distinct

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roles. The loss of regulation of the growth factor signalling pathway is a frequent occurrence in cancer as well as other disease states.

The signals mediated by kinases have also been shown to control growth, death and differentiation in the cell by regulating the processes of the cell cycle (Massague and Roberts, 1995). Progression through the eukaryotic cell cycle is controlled by a family of kinases called cyclin dependent kinases (CDKs) (Myerson et al., 1992). The regulation of CDK activation is complex, but requires the association of the CDK with a member of the cyclin family of regulatory subunits (Draetta, 1993; Murray and Kirschner, 1989; Solomon et al., 1992). A further level of regulation occurs through both activating and inactivating phosphorylations of the CDK subunit (Draetta, 1993; Ducommun et al., 1991; Gautier et al., 1989; Gould and Nurse, 1989; Krek and Nigg, 1991; Murray and Kirschner, 1989; Solomon et al., 1992; Solomon et al., 1990). The coordinate activation and inactivation of different cyclin/CDK complexes is necessary for normal progression through the cell cycle (Pines, 1993; Sherr, 1993). Both the critical G1-S and G2-M transitions are controlled by the activation of different cyclin/CDK activities. In G1, both cyclin D/CDK4 and cyclin E/CDK2 are thought to mediate the onset of S-phase (Matsushime et al., 1994; Ohtsubo and Roberts, 1993; Quelle et al., 1993; Resnitzky et al., 1994). Progression through S-phase requires the activity of cyclin A/CDK2 (Girard et al., 1991; Pagano et al., 1992; Rosenblatt et al., 1992; Walker and Maller, 1991; Zindy et al., 1992) whereas the activation of cyclin A/cdc2 (CDK1) and cyclin B/cdc2 are required for the onset of metaphase (Draetta, 1993; Girard et al., 1991; Murray and Kirschner, 1989; Pagano et al., 1992; Rosenblatt et al., 1992; Solomon et al., 1992; Walker and Maller, 1991; Zindy et al., 1992). It is not surprising, therefore, that the loss of control of CDK regulation is a frequent event in hyperproliferative diseases and cancer. (Hunter and Pines, 1994; Lees, 1995; Pines, 1992)

The kinase cRaf1 regulates cellular proliferation in two ways. The enzyme positively regulates cell division through the Raf/MEK/ERK protein kinase cascade. This activation is the result of cRaf1 catalyzed phosphorylation of the protein kinase, MEK1. MEK1 phosphorylates and activates the protein kinase ERK. ERK phosphorylates and regulates transcription factors required for cell division (Avruch et al, *TIBS*; 1994 (19) 279-283). cRaf1 negatively regulates cell death by modulation of the activity of Bcl-2, a critical regulator of apoptosis. This regulation involves direct phosphorylation of Bcl-2 family members (Gajewski and Thompson, *Cell*; 1996 (87) 619-628). Both of these aspects of cRaf1 mediated regulation of cellular proliferation require the kinase activity of cRaf1.

cRaf1 is deregulated by events that are common in human cancer. For example ras genes are mutated with the following frequencies in the following representative primary human tumors: lung (adenocarcinoma), 30%; colon (adenocarcinoma), 50%; pancreatic carcinoma, 90%; seminoma, 40%; thyroid, 50% (McCormick, *Ras oncogenes in Oncogenes and the molecular origins of cancer*; 1989, 125-146). cRaf1 is also activated by deregulation of tyrosine kinases including, cSrc, ErbB2, EGFR, and bcr/abl. These events are associated with breast, colon and lung carcinomas and chronic myelogenous leukemia (Fearon, *Genetic lesions in human cancer*, in *Molecular oncology*; 1996, 143-178). In addition, Raf anti-sense literature teaches that the reduction of Raf protein levels correlates with a reduction in tumor growth rate in in vivo tumor

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L3: Entry 21 of 23

File: USPT

Jul 31, 2001

DOCUMENT-IDENTIFIER: US 6268391 B1

TITLE: Benzylidene-1,3-dihydro-indol-2-one derivatives a receptor tyrosine kinase inhibitors, particularly of Raf kinases

Brief Summary Text (11):

Inhibitors of kinases involved in mediating or maintaining these disease states represent novel therapies for these disorders. Examples of such kinases include, but are not limited to: (1) inhibition of Src (Brickell, 1992; Courtneidge, 1994), raf (Powis, 1994) and the cyclin-dependent kinases (CDKs) 1, 2 and 4 in cancer (Hunter and Pines, 1994; Lees, 1995; Pines, 1992), (2) inhibition of CDK2 or PDGF-R kinase in restenosis (Buchdunger et al., 1995), (3) inhibition of CDK5 and GSK3 kinases in Alzheimers (Aplin et al., 1996; Hosoi et al., 1995), (4) inhibition of c-Src kinase in osteoporosis (Tanaka et al., 1996), (5) inhibition of GSK-3 kinase in type-2 diabetes (Borthwick et al., 1995); (6) inhibition of the p38 kinase in inflammation (Badger et al., 1996); (7) inhibition of VEGF-R 1-3 and TIE-1 and -2 kinases in angiogenesis (Shawver et al., 1997); (8) inhibition of UL97 kinase in viral infections (He et al., 1997); (9) inhibition of CSF-1R kinase in bone and hematopoietic diseases (Myers et al., 1997), and (10) inhibition of Lck kinase in autoimmune diseases and transplant rejection (Myers et al., 1997)